Isomorphism of Critical Phenomena in Liquid Mixtures and Cell-to-Cell Communication in Synapses

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Summary: Methods of the phase transition theory are used to study the cooperative phenomena of the synaptic transmission (cell-to-cell communication). A convenient approach to the process of cell-to-cell communication is commonly based on ideas about chemical intermediaries (transmitter agents) securing transmission between neurons in the synaptic cleft. This process has a cooperative behavior: about ten millions of transmitter molecules are releasing simultaneously under the influence of one nerve impulse.

A hypothesis is applied according to which the process of cell-to-cell communication in synapses for a system "intermediary-receptor" is isomorphic to the critical phenomena in binary liquid mixtures near the critical mixing point. Kinetic equations corresponding to the proposed scheme of chemical reactions inside synaptic clefts have a non-linear form. Using some special approximations it is possible to study the main characteristics of the process of cell-to-cell communication. Namely, the pair correlation functions and correlation length of order-parameter fluctuations are calculated for a system "intermediary-receptor" with restricted cylinder geometry of synaptic clefts taken into account. The temperature and concentration dependences of the activation zone as well as other parameters are examined at the post-synaptic membrane.

Introduction

The convenient theory of cell-to-cell communication is commonly based on ideas about chemical transmitters securing synaptic transmission between two neurons. Sequence of major events in cholinergic synapse is as follows:

1. Acetylcholine (ACh) – let us consider this transmitter – is synthesized and stored in spherical vesicles near the presynaptic membrane.

2. Then ACh releases and reacts with specific acetylcholine receptors in active state (R*).
3. The formation of the transmitter-receptor complex (ACh –R*) produces conformal changes in the postsynaptic membrane and therefore the in a membrane potential.
4. Finally ACh is either inactivated by acetylcholineesterase or is removed by diffusion.

It must be stressed that the process of ACh release is cooperative: about 10^7 ACh molecules are releasing simultaneously under the influence of one nerve impulse. Such a synchronous activation of large zone of receptors by ACh can be considered in details as the process that is isomorphic to the critical phenomena in binary liquid mixtures near the critical mixing point.

Kinetic equations

1. Kinetic equations for *concentrations x and y of receptors R* and acetylcholine-receptor complexes ACh-R** have the following form:

$$\begin{cases} \dfrac{dx}{dt} = k_2(1-x) - k_1 xy \\ \dfrac{dy}{dt} = f(t) - k_1 xy \end{cases}$$

where $f(t)$ is the source function describing the intensity of ACh release from spheroid vesicles, k_i are the coefficients of reactions velocities.

2. For stationary source function ($f = const$) the stationary points of these kinetic equations are

$x_s = 1-\varphi$, $y_s = \lambda\varphi/(1-\varphi)$, where $\lambda = k_2/k_1$ and $\varphi = f/k_2$.

It is important to stress that x_s does not depend on λ. It could be also seen that stationary value y_s of the ACh concentration is increasing to infinity when parameter φ is approaching 1. Physical sense has the situation when y_s changes in range from 0 to the critical value y_{crit}. In this case the source function

$f \le f_{\max} = \dfrac{y_{crit}}{1/k_1 + y_{crit}/k_2}$, where $f_{\max}$ gives the informational capability of the transmission channels.

Figure 1 shows the dependence of stationary points on parameters λ and φ.

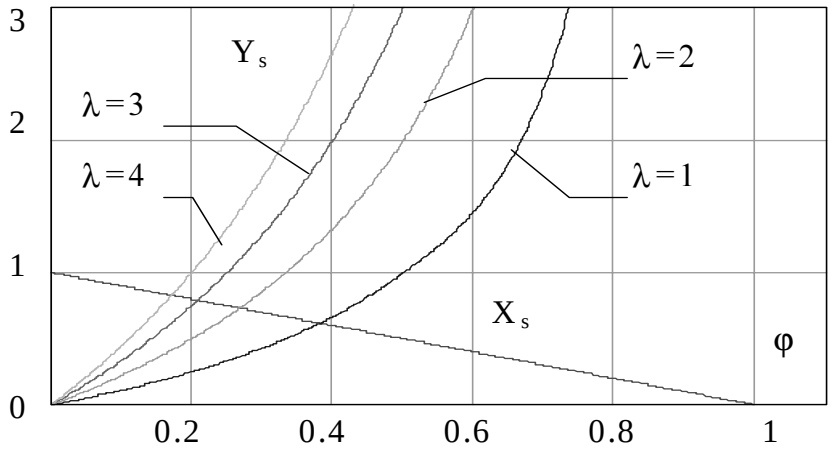

Fig. 1. Dependence of the stationary points on parameters λ and φ

3. For slow oscillations of the source function the system of kinetic equations for $x(\omega)$ and $y(\omega)$ is as follows:

$$\begin{cases} -i\omega x(\omega) = k_2\delta(\omega) - k_2 x(\omega) - k_1 x(\omega) y_0 - k_1 x''(\omega) y_2 \\ -i\omega y(\omega) = f(\omega) - k_1 x_0 y(\omega) - k_1 x_2 y''(\omega) \end{cases}$$

where $x_0 = \int x(\omega)d\omega$, $y_0 = \int y(\omega)d\omega$, $x_2 = \dfrac{1}{2}\int x(\omega)\omega^2 d\omega$, $y_2 = \dfrac{1}{2}\int y(\omega)\omega^2 d\omega$.

Solution of this system of differential equations has the form

$$x(t) = \frac{k_2}{k_1 y_2} G\left(t, \frac{k_2 + k_1 y_0}{k_1 y_2}, \frac{1}{k_1 y_2}\right), \quad y(t) = \frac{f(t) G\left(t, \frac{x_0}{x_2}, \frac{1}{k_1 x_2}\right)}{k_1 x_2} ,$$

where the function $G(t,\alpha,\beta) = \dfrac{\int \exp\left(-\frac{t^3}{3\beta} + \frac{\alpha}{\beta}t\right)dt}{\beta \exp\left(-\frac{t^3}{3\beta} + \frac{\alpha}{\beta}t\right)}$.

Thus, the source function $f(t)$ modulates the temporal evolution of the Ach-R* concentration.

The correlation function and activation zone for the process of synaptic transmission

For geometry of the restricted cylinder $0 \le \rho < a$, $-h \le z \le h$ with zeroth boundary conditions the *pair correlation function* of the system "mediator-receptor"

$$G_2(\rho, z) = \frac{1}{V} \cdot \sum_{n=0}^{\infty} \sum_{m=1}^{\infty} \frac{1}{J_1^2(\mu_m)} \frac{J_0(\mu_m \frac{\rho}{a}) \cos(\frac{\pi(n+0.5)z}{h})}{\kappa^2 + \frac{\pi^2 (2n+1)^2}{4h^2} + \frac{\mu_m^2}{a^2}}$$

where $J_0(x)$ is the Bessel function, μ_m is the solution of the equation $J_0(x) = 0$, $V = \pi a^2 h$ is the volume of the synaptic cleft. Next figures 2 and 3 demonstrate the behavior of the pair correlation function $G_2(\rho, z)$ in the synaptic cleft with parameters $a = 100$ nm and $h = 10$ nm.

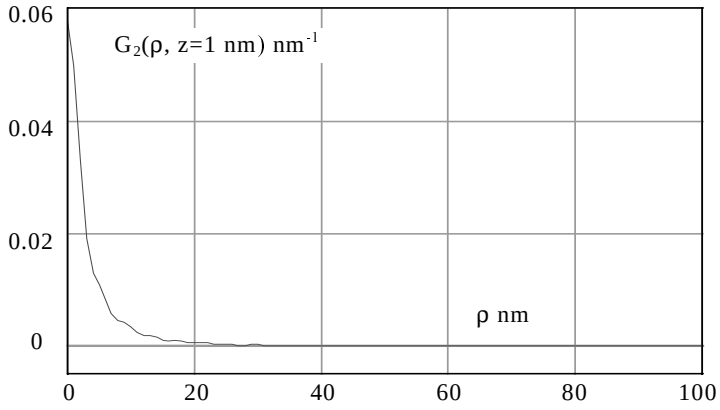

Fig. 2 . Dependence of the pair correlation function $G_2(\rho, z)$ on ρ

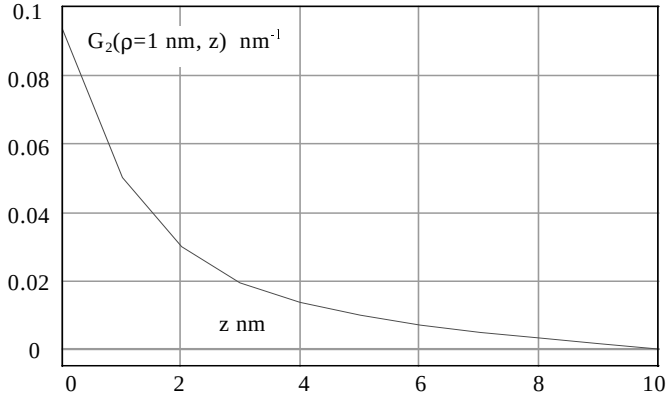

Fig. 3. Dependence of the pair correlation function $G_2(\rho, z)$ on z

The *correlation length* gives a linear size of the *activation zone* for the process of synaptic transmission

$$\xi = \sqrt{\frac{\sum_{n=0}^{\infty}\sum_{m=1}^{\infty} \frac{(-1)^n \left[a^2 \left(1 - \frac{2J_2(\mu_m)}{\mu_m J_1(\mu_m)}\right) + h^2 \left(1 - \frac{8}{\pi^2 (2n+1)^2}\right)\right]}{(2n+1)\mu_m J_1(\mu_m)\kappa_{nm}^2}}{\sum_{n=0}^{\infty}\sum_{m=1}^{\infty} \frac{(-1)^n}{(2n+1)\mu_m J_1(\mu_m)\kappa_{nm}^2}}},$$

where $\kappa_{nm}^2 = \kappa^2 + \frac{\pi^2 (2n+1)^2}{4h^2} + \frac{\mu_m^2}{a^2}$.

The temperature dependence of the correlation length (activation zone) is shown on the Figure 4 (with $\kappa_0 \cong 10^8 \ м^{-1}$ for the restricted cylindrical system).

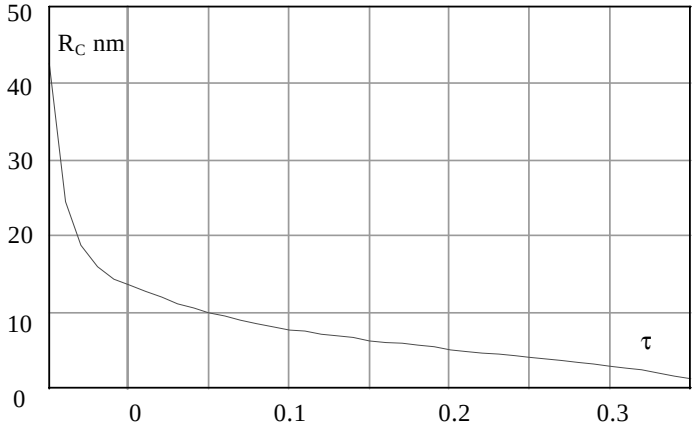

Fig. 4. The dependence of the correlation length on the temperature

The *shifts of the critical temperature* and *critical concentration*

$$\Delta T_C = \frac{T_C}{1 + \left(\sqrt{\frac{\pi^2}{K_1^2} + \frac{\mu_1^2}{K_2^2}} \right)^{-\frac{1}{\nu}}}, \qquad \Delta x_C = \frac{x_C}{1 + \left(\sqrt{\frac{\pi^2}{K_1^2} + \frac{\mu_1^2}{K_2^2}} \right)^{-\frac{\beta}{\nu}}} .$$

These shifts of the critical parameters depend on the geometrical factors $K_1 = 2h\kappa_0$ and $K_2 = a\kappa_0$. For example, if K_1 = 25 and K_2 = 125 then the shift of the critical temperature $\Delta T_C \approx$ 10 K while T_C = 300 K.

Conclusions

1. The stationary points of the concentration of R* and Ach-R* as well as the informational capability of the transmission channels depend on the kinetic coefficients. Therefore, changes in the temperature and influence of different external fields affect on the kinetic coefficients and as the result on the stationary points and the informational capability of the channels.
2. The source function (in the case of its slow oscillatory behavior) modulates the temporal evolution of the Ach-R* concentration.
3. The correlation length determines the zone of reagents activation. It depends on the geometric factor of the cleft and on the temperature as well. So conformal changes of the geometrical form of the synaptic cleft and shifts of the temperature affects on the activation zone.
4. As the result of the space limitation, shifts of the critical temperature and density take place. Their dependence on the geometric factor must be taken into account while studying isomorphism of critical phenomena in confined liquid mixtures and cell-to-cell communication in synapses.

References

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